In the United States Court of Federal Claims

No. 12-87V

(Filed Under Seal: December 27, 2019 | Reissued: April 6, 2020)[*]

LISA FAUP, as Parent of A.F., a minor, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Keywords: Vaccine Act; Motion for Review; Systemic Juvenile Idiopathic Arthritis (sJIA); Diphtheria-Tetanus-acellular-Pertussis (DTaP) Vaccine; Inactivated Polio (IP) Vaccine; Althen Causation.

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Catherine E. Stolar, Trial Attorney, Torts Branch, Civil Division, U.S. Department of Justice, with whom were *Gabrielle M. Fielding*, Assistant Director, *Catharine E. Reeves*, Deputy Director, *C. Salvatore D'Alessio*, Acting Director, *Joseph H. Hunt*, Assistant Attorney General.

OPINION AND ORDER

KAPLAN, Judge.

The Petitioner, Lisa Faup, seeks review of a decision dismissing a petition for compensation issued under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§300aa-1 to -34 (the "Vaccine Act" or "the Act"), as amended, that she filed on behalf of her daughter, A.F. Dec. on Entitlement, Faup v. Sec'y of Health & Human Servs., No. 12-87V (Fed. Cl. Spec. Mstr. June 17, 2019), ECF No. 120 (hereinafter the "Decision" or "Dec."). The Special Master dismissed the petition based on her conclusion that Petitioner failed to show that the Diphtheria-Tetanus-acellular-Pertussis ("DTaP") and inactivated polio ("IP" or "polio") vaccines A.F. received on March 13, 2009 caused A.F. to develop systemic Juvenile Idiopathic Arthritis ("sJIA").

In her motion for review, Petitioner contends that: 1) the Special Master improperly heightened her burden of proof by requiring her to prove the validity of the so-called

[*] This opinion was previously issued under seal on December 27, 2019. The parties were given the opportunity to propose redactions on or before January 10, 2020. Because the parties have not filed proposed redactions, the Court reissues its decision in its entirety.

"Autoimmune (auto-inflammatory) Syndrome Induced by Adjuvants" theory ("ASIA"), notwithstanding that her experts' actual theory was a narrower one specific to A.F.'s medical history and injury; 2) she ignored some of Petitioner's evidence regarding causation; and 3) her decision was not based on the record as a whole. In response, the government argues that the Special Master applied the correct evidentiary standards and that the record supports the conclusions she reached regarding Petitioner's failure to establish causation.

The Court agrees with Petitioner that the Special Master's decision reflects some conflation of Petitioner's specific theory of causation with the more generic ASIA theory. The Special Master's error in that regard, however, was a harmless one because the Special Master's decision also demonstrates that she rationally concluded based on the evidence before her that: 1) Petitioner had failed to prove by preponderant evidence the viability of her experts' specific theory of causation; and 2) it was more likely that A.F.'s sJIA was triggered by a viral infection than her vaccinations. The Court further finds unpersuasive Petitioner's arguments that the Special Master ignored relevant evidence and/or that her decision was not based on the record as a whole. In light of the deference the Court owes to the findings and credibility determinations of special masters under the Vaccine Act, Petitioner's motion for review must be **DENIED**.

BACKGROUND

I. Medical History

A.F. was born prematurely on March 9, 2004, the oldest of a set of triplets. Pet'r's Ex. 1 at 1, 22–23, ECF No. 8-1. She showed no signs of any lasting health concerns at birth. Id. At seven weeks of age, A.F. was diagnosed with an "innocent heart murmur" but was found "otherwise normal" by a pediatric cardiologist. Id. at 27–28. A.F. received all of her early immunizations without incident. Id. at 2.

On March 2, 2009, a pediatrician diagnosed A.F. with an ear infection, known as otitis media, and prescribed a seven-day course of amoxicillin, an antibiotic. Pet'r's Ex. 15 at 1, ECF No. 10-1; Pet'r's Ex. 1 at 72. Several days later, on March 13, A.F. received her regular DTaP and polio vaccines. Pet'r's Ex. 15 at 1.

On March 20, A.F. visited her pediatrician for a maculopapular rash[1] that had developed on or around March 17. Id.; Pet'r's Ex. 1 at 16. While at her pediatrician's office, A.F. did not have a fever and tested negative for strep throat. Pet'r's Ex. 1 at 16; Pet'r's Ex. 11 at 2, ECF No. 8-11. She received prednisone for the rash. Pet'r's Ex. 15 at 1. A pediatric note from that same day stated that A.F. "[complains of] . . . [left] elbow [and] wrist pains." Id. On March 25, A.F.'s symptoms had worsened, and she returned to her pediatrician for abdominal pain, a swollen elbow, a painful knee and ankles, and a recurring fever of up to 104 degrees Fahrenheit. Pet'r's Ex. 1 at 16. Her pediatrician considered a diagnosis of Henoch-Schönlein purpura ("HSP").[2]

[1] A maculopapular rash is one characterized by "both flat and raised skin lesions . . . [which] are usually red and can merge together." Dec. at 3 n.7.

[2] Henoch-Schönlein purpura is "a form of nonthrombocytopenic purpura, sometimes a type of hypersensitivity vasculitis and sometimes of unknown cause, usually seen in children and

Pet'r's Ex. 15 at 1. On March 27, A.F. saw an allergist who could not determine whether A.F.'s rash was allergic or viral but gave her Benadryl to rule out an allergy. Pet'r's Ex. 3 at 3, ECF No. 8-3. The allergist recommended that A.F. go to the emergency room. Id.

A.F. was admitted to the emergency room at Robert Wood Johnson University Hospital later that day, where it was noted that she had an itchy "maculopapular rash to her face, trunk, and extremities, slightly raised, [with] some rashes to her ankles [that were] darker in color[,] slightly brown and discolored," and that she experienced "mild difficulty walking due to discomfort." Pet'r's Ex. 2 at 2, ECF No. 8-2. The rash on her "lower extremity" was described as "with petechia[3] and purpura."[4] Id. at 4. A.F.'s mother reported that A.F. had a "fever intermittently over the past 6 days" and that the rash started about ten days earlier as "'itchy small pink bumps' over [her] extremities and buttocks, [which] spread to [the] rest of [her] body." Id. at 2. A.F. was diagnosed with HSP and discharged the same day. Id. at 1.

On March 31, A.F. saw an infectious disease specialist at Richmond Pediatrics presenting with a fever, joint pain, a rash, difficulty walking, and loss of appetite. Pet'r's Ex. 4 at 1, ECF No. 8-4. She returned to the same specialist on April 8 and reported a temperature of "102-104 since Saturday . . . [, painful] joints . . . [,] and [swollen] wrists and hands." Id. at 2. The specialist documented an impression of "Viral vs. [Juvenile Rheumatoid Arthritis], HSP." Id.

On April 16, A.F. was seen by Dr. Yukiko Kimura, a pediatric rheumatologist, for an initial evaluation. Pet'r's Ex. 5 at 1, ECF No. 8-5. At that time, A.F. "appeared well" and had not complained of pain for several days. Id. She reported a continuous itchy rash, however, which worsened when she had a fever. Id. The prednisone prescribed on March 26 "did not seem to help with the fever," although Motrin "seem[ed] to help quite a bit." Id. In a letter summarizing her evaluations, Dr. Kimura reported that A.F. "received a DTaP/[I]PV on 3/13/09 [and s]he was also treated with amoxicillin for [otitis media] on 3/2 for 7 days." Id. Dr. Kimura characterized A.F.'s rash as "the classic rash of systemic [Juvenile Idiopathic Arthritis ("sJIA")] on her face, arms and legs." Id.[5] The doctor's "impression at that time was that [A.F.] most likely had

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associated with symptoms including urticaria, erythema, arthopathy, arthritis, gastrointestinal symptoms, and renal involvement." Dorland's Illustrated Medical Dictionary at 1557 (32nd ed. 2012) (hereinafter "Dorland's").

[3] Petechia is "a pinpoint, nonraised, perfectly round, purplish red spot caused by intradermal or submucous hemorrhage." Dorland's at 1422.

[4] Purpura is defined as "any of a group of conditions characterized by ecchymoses or other small hemorrhages in the skin, mucous membranes, or serosal surfaces; causes include blood disorders, vascular abnormalities, and trauma." Dorland's at 1557.

[5] Juvenile idiopathic arthritis is a type of "rheumatoid arthritis in children, [characterized by] swelling, tenderness, and pain in one or more joints, which may lead to impaired growth and development, limitation of movement, ankylosis, and flexion contractures." Dorland's at 150. Systemic onset juvenile idiopathic arthritis is "a form of juvenile idiopathic arthritis

systemic JIA, but that she appeared to be improving without treatment." Id. at 2. Accordingly, Dr. Kimura asked A.F.'s mother "to keep a detailed fever and symptom diary," id., and directed her to give A.F. Motrin or Naprosyn if her fever or joint pain reappeared, id. at 9. A.F. went to a follow-up appointment with Dr. Kimura two weeks later on April 28 and reported "only two days of fever the previous week, and [that she] was otherwise OK except for some joint pain." Id. at 2.

For several weeks after that appointment, A.F.'s mother reported that A.F. "seemed to do well except for [a] rash[, with] no fever or joint pain." Id. The weekend of May 8, however, A.F. had a severe flare up of her rash and joint pain and developed a high fever. Id. Dr. Kimura prescribed naproxen, "which improved her symptoms." Id.

Early in the week of May 18, A.F. "developed fever and rash at the time that one of her siblings had strep, and Mrs. Faup started her on amoxicillin." Id. A.F.'s mother characterized this rash as a "strep rash" that was "different from the JIA rash." Id. A.F. had lab work done on May 26, which "showed possible MAS (macrophage activation syndrome—a hemophagocytic syndrome that can be life threatening in systemic JIA)." Id. Dr. Kimura reported that the "fever and rash episode that she had early in the week may have been MAS." Id. Dr. Kimura advised petitioner that "MAS is a life threatening complication of [s]JIA that can flare at any time, and that [A.F.] most likely needs steroids or a biologic agent that blocks IL-1, which has been shown to be very effective in treating children with systemic JIA." Id.

Immediately after A.F.'s alarming lab results came in on May 27, A.F.'s mother was advised to take her daughter to the hospital to have the labs repeated immediately. Id. Although A.F. had no symptoms at this time, with no fever, rash, or joint pain, A.F.'s mother took A.F. to the Children's Hospital of Philadelphia emergency department on May 28. Id.; Pet'r's Ex. 12 at 1, ECF No. 8-12. Rheumatology assessed A.F.'s condition and concurred with the diagnosis of sJIA. Pet'r's Ex. 12 at 12. The repeated lab work "showed some improvement (from 5/27)," and A.F.'s mother was asked to keep a close eye on A.F. and take her immediately to the emergency room if her symptoms worsened. Pet'r's Ex. 5 at 2.

On June 4, A.F. remained largely asymptomatic, but had a bone marrow evaluation done to rule out leukemia or MAS. Pet'r's Ex. 1 at 65. This test was "normal and showed no evidence of either malignancy or MAS." Id. A.F. attended a follow-up appointment with Dr. Kimura the same day. Id. at 66. Dr. Kimura opined that A.F.'s MAS episode from May had "spontaneously improved since she [was] asymptomatic at this time." Pet'r's Ex. 5 at 2. Dr. Kimura documented that A.F. had swelling in both ankles, a rash, a low-grade fever, and "occas[ional] joint pain." Pet'r's Ex. 1 at 66–67. Dr. Kimura assessed that A.F.'s sJIA was "still active" although her "[status post] MAS [was] self controlled." Id. at 67. On June 16, A.F. saw Dr. Kimura for "some rash [and] occas[ional] joint pain," although she had not had a fever since her last visit. Id. at 46. A.F. began treatment with methotrexate, id., a drug "used as an antipsoriatic and antiarthritic in the treatment of . . . severe rheumatoid and psoriatic arthritis," Dorland's at 1151.

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accompanied by systemic manifestations such as spiking fever, transient rash on the trunk and limbs, hepatosplenomegaly, generalized lymphadenopathy, and anemia." Id. at 157.

On June 17, 2009, Petitioner took A.F. for an assessment by Dr. Thomas Lehman, another pediatric rheumatologist. Pet'r's Ex. 6 at 1–2. Although her symptoms had greatly improved, Dr. Lehman found that A.F. "ha[d] clearly documented systemic-onset [juvenile rheumatoid arthritis] by history and laboratory findings," confirming her sJIA diagnosis by Dr. Kimura. Id. at 2.[6]

A.F. returned to see Dr. Kimura multiple times between July 14, 2009 and July 13, 2010. Pet'r's Ex. 1 at 43, 49, 52, 55, 58. Throughout this period, A.F.'s symptoms continued to dramatically improve, until on July 13, 2010, A.F. reported no symptoms at all since her last visit. Id. at 58. Around July 16 of 2009, Dr. Kimura advised Petitioner to stop the Naprosyn, and around June 1, 2010, A.F. stopped taking the methotrexate without any resurgence in symptoms. Id. at 44, 58–59. Although A.F.'s lab results continued to be abnormal, A.F. remained healthy with no return of her sJIA symptoms. Pet'r's Ex. 5 at 78–79; Pet'r's Ex. 18 at 4, ECF No. 18-1.

II. Procedural Background

A. Pre-Hearing Proceedings Before the Special Master

On February 9, 2012, Petitioner filed a petition alleging that the vaccinations that A.F. received on March 13, 2009 caused her to suffer "rheumatologic injury." Pet. For Vaccine Compensation at ¶¶ 1–2, ECF No. 1. In February and April of 2012, Petitioner submitted A.F.'s medical records for consideration in connection with her petition. ECF Nos. 8, 10.

On June 18, 2012, the Secretary of Health and Human Services filed a Rule 4(c) Report, recommending against compensation on the grounds that, in relevant part, Petitioner had failed to proffer a medical theory causally linking A.F.'s injuries with the vaccines she received on March 13, 2009. See Resp't's Rule 4(c) Report at 1, 14, ECF No. 12.

On September 12, 2013, Petitioner submitted an expert report prepared by Dr. Robert Sundel, M.D., a pediatric rheumatologist, along with his curriculum vitae and supporting literature. ECF No. 30. Petitioner submitted Dr. Sundel's first supplemental expert report on June 15, 2015, ECF No. 44, and his second supplemental expert report on February 5, 2016, ECF No. 51. On February 13, 2017, Petitioner filed an expert report from Dr. Michael Gurish, a Ph.D. in Experimental Pathology (Immunology). ECF No. 76.

The government submitted an expert report from Dr. Carlos Rose, M.D., C.I.P, a pediatric rheumatologist, on January 13, 2014, along with his curriculum vitae and supporting articles. ECF No. 32. On August 14, 2015, the government filed the first supplemental expert report of Dr. Rose, along with expert reports from Dr. Edward W. Cetaruk, M.D., and Dr. J. Lindsay Whitton, M.D., Ph.D. ECF No. 45. The government submitted Dr. Whitton's first supplemental expert report on August 4, 2016, ECF No. 60, and his second supplemental expert report on May 30, 2017, ECF No. 86.

[6] Systemic juvenile idiopathic arthritis (JIA) and systemic juvenile rheumatoid arthritis (JRA) are the same condition. See Dorland's at 157 (providing the same definition for JIA and JRA).

B. The Entitlement Hearing

An entitlement hearing was held in Washington, D.C. on March 13–14, 2018. ECF Nos. 114, 115. At the hearing, both parties presented the testimony of their experts, which is summarized below.

1. Petitioner's Experts[7]

a. Opinion of Dr. Robert Sundel

i. Overview

Dr. Robert Sundel, a pediatric rheumatologist, submitted three expert reports in this case and testified at the entitlement hearing. In his opinion, the DTaP and polio vaccines administered on March 13, 2009 were the most likely cause of A.F.'s sJIA.

Although the pathogenesis of sJIA is unknown, Dr. Sundel postulated during his testimony that its cause is likely "multifactorial," Tr. 27:6–10, ECF Nos. 114, 115, involving "a multitude of environmental, genetic and epigenetic factors," Pet'r's Ex. 24 at 3, ECF No. 51-1 (Second Supplemental Expert Report of Dr. Sundel). Dr. Sundel opined that A.F. developed sJIA because of her "genetic susceptibility, [the] stimulation of [her] immune system, and the[immunization which served as the] one final jerk to the immune system." Tr. at 304:17–18, 303:16–20.

Dr. Sundel based his theory of causation on the "common understanding today [that s]JIA is an innate immune system inflammatory disorder [("autoinflammatory disease")]." Id. at 37:8–9. The innate immune system, Dr. Sundel testified, is the system's first responder, id. at 28:6–8, yet it is the "more primitive" arm of the immune system, id. at 28:17. "[I]t has the advantage of working quickly and taking care of most of the major early pathogens." Id. at 28:17–19. It does so by "rapidly identify[ing] and destroy[ing]" invading organisms. Id. at 28:6–8. After the innate immune system gets to work, Dr. Sundel explained, the adaptive arm of the immune system takes over, which "changes its response depending on the exact invader, and also adjusts its attack on the invader over time." Id. at 28:9–11. Dr. Sundel explained that "innate [immune] responses . . . , occur more rapidly than adaptive [immune] responses—minutes to hours rather than . . . days to weeks." Pet'r's Ex. 24 at 2.

Implicated in the innate immune system, sJIA, and MAS, according to Dr. Sundel, are monocytes, the cytokine[8] "IL-18," and the cytokines "IL-1 and IL-6 . . . that cause fever and . . . inflammation." Tr. at 31:6–13. These "markers of the innate immune system are abnormal in [s]JIA." Id. at 31:6–16. Monocytes, he explained, "can become macrophages," which in turn are

[7] For a recitation of the qualifications of Petitioner's and the government's expert witnesses, see Dec. at 7–16.

[8] Cytokine is the "generic term for nonantibody proteins released by one cell population . . . on contact with specific antigen, which act as intercellular mediators, as in the generation of an immune response." Dorland's at 466.

primarily responsible for "releasing the cytokines in [MAS]" and are one component of the body's innate immune response. Id. at 31:24–32:21. "IL-18," he further explained, "is the central cytokine in the innate immune system," id. at 40:3–5, and it is "much higher in [s]JIA and higher still in [MAS]" than it is in other inflammatory diseases or infections, id. at 48:6–8. Thus, Dr. Sundel testified, it is unsurprising that a "significant percentage" of patients with sJIA also suffer from MAS, and "high levels [of IL-18] are predictive . . . of developing MAS." Id. at 39:23–40:8. MAS, Dr. Sundel explained, is a "cytokine storm . . . [,] where the innate immune system[] and . . . the adaptive immune system[] are all triggered simultaneously." Id. at 38:22–39:3. The immune system is overwhelmed, he stated, which causes multiple dangerous symptoms, including fever. Id. at 39:3–7, 39:19–22.

Autoinflammatory diseases, Dr. Sundel testified, are characterized by a dysregulation of the innate immune system's ability to respond, specifically "poor control of inflammation [where] . . . the normal mechanisms by which the body [controls and prevents inflammation] continually [do not] work." Id. at 30:16–20. Therefore, Dr. Sundel concluded, "fever and rashes and arthritis [occur] in children with systemic JIA, because their innate immune system is . . . out of control." Id. at 30:22–24.

Dr. Sundel explained that systemic JIA involves "systemic features of inflammation" in addition to inflammation of the joints. Id. at 26:13–16. SJIA must be "diagnosed clinically" as its cause is unknown, and it has "numerous manifestations that can differ from child to child." Id. at 26:18–22. A.F.'s symptoms supportive of her sJIA diagnosis, Dr. Sundel testified, were her rash, fever, arthritis, enlarged liver and spleen, and swollen lymph nodes. Id. at 26:24–27:5.

SJIA is triggered, according to Dr. Sundel, when a "genetically susceptible host[]," Pet'r's Ex. 20 at 2, ECF No. 30-1 (Expert Report of Dr. Sundel),[9] experiences "low-grade inflammation that is controlled and then [some trigger] increases the amount of inflammation in the child, the child is no longer able to maintain control of this low-grade inflammation and . . . it explodes into a case of [s]JIA," Tr. at 27:15–21.

Dr. Sundel's theory is based at least partially on the fact that the DTaP vaccine contains an aluminum adjuvant ("aluminum" or "alum"). See id. at 45:4–5.[10] Adjuvants, Dr. Sundel testified, are intentionally designed to "stimulate[]" the innate immune response. Id. at 34:24–25. Dr. Sundel posited that adjuvants "activate[] the inflammasomes, which are the control center[s] of the innate immune system, causing release of [the] IL-18 [cytokine], and trigger[ing] . . . inflammation . . . in the innate immune system." Id. at 34:24–35:4. Dr. Sundel also explained that the innate immune system "is built to recognize" another primary component of a vaccine, the antigen, so that the immune system launches "a speedy attack . . . mediated by the innate

[9] For Pet'r's Ex. 20, the Court uses the pagination of the PDF document from the CM-ECF system.

[10] An adjuvant is defined as "a substance that aids another," or, "in immunology, a nonspecific stimulator of the immune response, such as BCG vaccine." Dorland's at 32. More specifically, Dr. Sundel explained that "[a]djuvants, particularly aluminum[,] . . . are additives used to increase the immunologic response to vaccines." Pet'r's Ex. 24 at 4.

immune system." Id. at 34:2–7.[11] But while he concluded that A.F.'s sJIA "could[not] have happened without the vaccine," id. at 88:6–8, he stated that there was not "enough data" to pinpoint specifically which part of the vaccine (i.e., the adjuvants or the antigen) caused her sJIA, id. at 87:24–25, and he did not know "[w]hether it was essential to have all aspects of the . . . vaccine," id. at 310:19–21.

ii. Dr. Sundel's Discussion of "ASIA"

Of significance to the issues raised in the motion for review, Dr. Sundel's expert reports also contained references to research concerning what has been characterized as the "Autoimmune (auto-inflammatory) Syndrome Induced by Adjuvants" (also known as "ASIA"). See Pet'r's Ex. 23 at 3–4, ECF No. 44-1 (First Supplemental Report of Dr. Sundel).[12] The existence of that syndrome was first proposed in an article published in 2011 in the Journal of Autoimmunity. See Pet'r's Ex. 23, Tab D (Yehuda Shoenfeld & Nancy Agmon-Levin, 'ASIA' – Autoimmune/inflammatory syndrome induced by adjuvants, 36 J. Autoimm. 4 (2011) (hereinafter the "Shoenfeld article"). The article's authors, Drs. Shoenfeld and Agmon-Levin, hypothesized that a "genetically susceptible subject may develop an autoimmune or auto-inflammatory disease . . . following exposure" to an "adjuvant." Id. at 37. They also posited that "in rare occasions, . . . vaccines can induce . . . enigmatic inflammatory condition and overt autoimmune disease . . . weeks and even months or years following vaccination." Id. at 38. Drs. Shoenfeld and Agmon-Levin recommended that four different medical conditions that "share clinical and pathogenic resemblances . . . be included under a common syndrome entitled the 'Autoimmune (Auto-Inflammatory Syndrome Induced by Adjuvants' (ASIA)." Id. at 40. These allegedly related medical conditions included siliconosis, Gulf War syndrome, macrophagic myofascitis syndrome, and a variety of "post-vaccination phenomena." Id. at 37. The article proposed several major and minor criteria that would justify an ASIA diagnosis. Id. at 40.

In his first supplemental expert report, Dr. Sundel included several references to the ASIA theory, observing that it has "raised the possibility that triggering of arthritis and other forms of autoimmunity may be the result of immune potentiation by additives to immunizations rather than the vaccines themselves." Pet'r's Ex. 23 at 4 (citing Pet'r's Ex. 23, Tab D (Shoenfeld article)). He also wrote that A.F.'s "arthritis is consistent with the . . . rapid response that may occur when [an] adjuvant triggers pathologic inflammation," and that the "[d]ata supporting such a mechanism in the pathogenesis of post-vaccination phenomena" was summarized in the Shoenfeld article. Id. at 4. Dr. Sundel also cited an article, which attempted to test the ASIA hypothesis, as "support[ing] a role of aluminum adjuvants particularly in young girls who develop arthritis shortly after an immunization." Id. at 5 (citing Pet'r's Ex. 23, Tab L (Sergio

[11] An antigen is "any substance capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response . . . [and] may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells." Dorland's at 103.

[12] For Pet'r's Ex. 23, the Court uses the pagination of the PDF document from the CM-ECF system.

Cerpa-Cruz et al., Adverse Events Following Immunization with Vaccines Containing Adjuvants, 56 Immunol. Research 299 (2013)).

Dr. Sundel did not bring up the ASIA theory in his direct testimony, but it was raised by counsel for the government in her cross-examination. In response to her questions, he characterized ASIA as "an overly broad generalization of what happens with vaccines." Tr. at 72:5–6. Nonetheless, he stated that the ASIA theory had value because it showed "[t]hat we had not been paying enough attention to what the adjuvants do, and we had not been considering possible adverse effects." Id. at 74:9–11. "[T]hroughout history," he continued, "vaccines have had both good and bad effects, and the relative number of good and bad effects vary, and over time, the claims that certain good or bad effects are caused by the vaccines are proven or disproven by scientists." Id. at 74:11–16. He stated that while the Shoenfeld article was "not proof," it provided "a reasonable hypothesis that in some patients [adjuvants have] an adverse effect." Id. at 83:9–11.

The Special Master also questioned Dr. Sundel regarding his understanding of ASIA. He characterized ASIA as "a general theory that there can be adverse effects from the effects of adjuvants on people, basically, very broadly," and observed that it was "too broad for a theory that will have any use in clinical medicine, or even in the legal system." Id. at 84:18–22. Upon further questioning by the Special Master, he also stated that another difference between his theory and ASIA is that he was unsure whether it was the adjuvant, an antigen, or a combination that caused A.F.'s sJIA. Id. at 88:10–13. He stated that "[i]t couldn't have happened without the vaccine," although he really did not know "was it the IP [vaccine], was it the DTaP, was it alum?" "[B]ut," he said, "I do know that the combination was not good for her." Id. at 88:5–9.

b. Opinion of Dr. Michael Gurish

Dr. Michael Gurish, a Ph.D. in Experimental Pathology (Immunology), submitted one expert report and testified at the entitlement hearing. Dec. at 10.[13] Dr. Gurish agreed with Dr. Sundel that "[t]here is good reason to believe the adjuvanted Diphtheria and Tetanus vaccine induced or provoked the inflammatory response that led to the appearance of [A.F.'s] sJIA." Pet'r's Ex. 29 at 1, ECF No. 76-1 (Expert Report of Dr. Gurish).

At the entitlement hearing, Dr. Gurish began his testimony by explaining, as had Dr. Sundel, that "the immune system [is] divided into the innate versus the adaptive immune system." Tr. at 96:23–24. Dr. Gurish described the innate immune system as "the first to be activated" in an immune response, id. at. 97:16–18, "which then stimulates the adaptive immune system . . . by presenting components (antigens) of the pathogens . . . and by their secretion of mediators (cytokines)," Pet'r's Ex. 29 at 2. In his expert report, Dr. Gurish observed that sJIA is an "autoinflammatory reaction," meaning that it "principally involves innate cells, such as

[13] Dr. Gurish is also an associate immunochemist at Brigham and Women's Hospital in Boston, and an associate professor of medicine at Harvard Medical School. Dec. at 10. The Special Master noted that Petitioner "did not move to admit Dr. Gurish as an expert in the field of immunology," but that "he provided opinion testimony in that area." Id. at 11.

macrophages." Id. In A.F.'s case, Dr. Gurish wrote, "it appears that [her] innate immunity was over stimulated and uncontrolled because [A.F. also] experienced [MAS]." Id. at 3.

Dr. Gurish testified that—in combination with a number of other factors, such as A.F.'s previous ear infection and recent treatment with antibiotics—the alum from the vaccine "stimulate[d A.F.'s] immune system" and set off a chain of internal immune responses that led to the "robust innate activation" that ultimately triggered A.F.'s sJIA. Tr. at 114:24–115:4. Dr. Gurish explained that "alum . . . forms a complex" that "activates the macrophage and induces the formation of inflammasomes." Id. at 105:14–16, 105:24–106:2. In turn, "the formation of the inflammasome" produces "cytokines," such as "IL-1 and IL-18." Id. at 106:6–15. The "subsequent elaboration of cytokines such as IL-1 and IL-6," Dr. Gurish wrote in explanation, are "two of the most important mediators of sJIA." Pet'r's Ex. 29 at 4.

2. The Government's Experts

a. Opinion of Dr. Carlos Rose

Dr. Carlos Rose, a pediatric rheumatologist, submitted two expert reports and testified at the entitlement hearing, where he evaluated and criticized Petitioner's vaccine-induced theory of causation and posited an alternative theory of viral causation to explain why A.F. developed sJIA. Dr. Rose agreed with Petitioner's experts on a number of points relating to sJIA's characterization as an autoinflammatory disease and the immunologic effects of adjuvants on the body. But he concluded that—contrary to Petitioner's experts—the vaccine played no role in the onset of A.F.'s sJIA. Tr. at 141:19–22. Rather, he opined that the cause was more likely viral in origin, encompassing both the viral ear infection that preceded the vaccination and a possible exposure to an undiagnosed viral infection "between vaccin[ation] and [the] onset of [her s]JIA." Resp't's Ex. G at 2, ECF No. 45-1 (First Supplemental Expert Report of Dr. Rose). Dr. Rose reasoned that if the vaccines had caused "a clinical and relevant activation of the innate immune system," then he thought A.F. should have had "at least some fever . . . within . . . 24 or 48 hours" after she was vaccinated. Tr. at 160:1–6.

b. Opinion of Dr. James Whitton

Dr. James Whitton, an immunologist, submitted three expert reports and testified at the entitlement hearing. In his first supplemental expert report, Dr. Whitton proposed that A.F.'s sJIA was triggered by her previous ear infection, whose "[b]acterial DNA is a strong stimulator of the innate immune response." Resp't's Ex. J at 11, ECF No. 60-1 (First Supplemental Expert Report of Dr. Whitton). He also "note[d] with interest Dr. Rose's contention that the purpuric rash that she displayed early in the course of disease might have been reflective of an undiagnosed viral infection." Id.

Like Dr. Rose, Dr. Whitton agreed with Petitioner's experts overview of the basic mechanics of aluminum's activation of the innate immune system, Tr. at 201:14–17, and sJIA's characterization as an autoinflammatory disease, id. at 238:1–3, 15–18. But the fact that "alum will be taken up by macrophages and cause a local inflammatory response," Dr. Whitton warned, should not be "conflate[d]" with the notion that this can "cause an autoimmune disease." Id. at 260:1–13. He disagreed with Petitioner's theory of vaccine-induced causation based primarily on

his opinion that the triggering of the innate immune system that results from alum, including the production of cytokines, is of limited duration, id. at 201:17–202:4, occurring "usually within the first 24 to 48 hours and [then] dissipat[ing] fairly rapidly thereafter," id. at 202:15–20. In Dr. Whitton's view, an "ongoing driver" of inflammation is required to "drive a serious autoinflammatory disease," and the relatively short-lived activation of the innate immune system that occurs in response to an alum adjuvant does not provide such a driver. Resp't's Ex. J at 8–9 (internal quotation marks omitted).

C. The Special Master's Decision

Following the hearing, the parties submitted post-hearing briefs. ECF Nos. 116, 118, 119. On June 17, 2019, the Special Master issued a decision ruling that A.F. was not entitled to compensation under the Vaccine Act because Petitioner failed to show that A.F.'s condition was caused by the vaccines. ECF No. 120.

1. Credibility of Petitioner's Experts

The Special Master began her analysis with a general critique of the credibility of Petitioner's experts, Drs. Sundel and Gurish. She acknowledged Dr. Sundel's "impressive credentials" and his extensive experience treating sJIA patients but found that his expertise "was undercut" by what she characterized as "a vague and inconsistent causation theory." Dec. at 28. Among other things, she found it significant that despite his "clear assertion that sJIA is an autoimmune syndrome induced by adjuvants," Dr. Sundel had "not refer[red] to his theory by the ASIA acronym well known in the [Vaccine] program." Id.[14]

The Special Master acknowledged that Dr. Sundel had disavowed reliance on the ASIA theory during his testimony, and that he had stated that, in his view, ASIA is "too broad for a theory that will have any use in clinical medicine, or even in the legal system." See id. at 28 (quoting Tr. at 84:20–22). But the Special Master considered his "rejection of ASIA . . . contradicted by his filed medical literature," in particular by: 1) his citation of the Cerpa-Cruz article, supra, as his "best evidence that aluminum salt adjuvant can trigger pathologic inflammation or another adverse event," and 2) the citation of the Shoenfeld article in his expert report and his statements under questioning by the Special Master in which he "praised Dr. Shoenfeld's work while acknowledging that it needs to be understood better," and "conceded" that the 2011 article "is not proof," id. (internal quotation marks and citations omitted).

"For many of the same reasons," the Special Master also found Dr. Gurish unpersuasive. Id. at 29. Specifically, she observed that Dr. Gurish—who, like Dr. Sundel, had disavowed reliance upon ASIA as the basis for his theory of causation—had failed to "explain how he had

[14] The Special Master's reference to ASIA as being "well-known" in the vaccine program is based on several decisions that she discussed subsequently in her opinion, in which, she stated, its validity was "called into doubt." Dec. at 29.

narrowed Dr. Shoenfeld's ASIA theory"; nor had he "explained away holes in the [ASIA] causation theory that relate to its vague symptoms or unspecified triggers." Id. at 28–29.[15]

2. Althen Prong One

The Special Master then analyzed whether Petitioner had met her burden to prove by a preponderance of the evidence that the vaccine caused her injury using the three-prong test set forth in Althen v. Secretary of Health and Human Services. 418 F.3d 1274 (Fed. Cir. 2005). Turning to Althen prong one, the Special Master concluded that Petitioner "failed to prove by a preponderance of the evidence her theory causally connecting A.F.'s DTaP and IP vaccinations to her sJIA." Dec. at 29. She noted that Dr. Sundel's theory was constructed on the basis of sJIA's characterization as an autoinflammatory disease, "the general principles of the innate immune system, and the accepted premise that the DTaP and IP vaccines are designed to elicit an immune response." Id.

The Special Master stated that Petitioner's medical theory "can best be summed up by Dr. Sundel's assertion, "was it the IP[vaccine], was it the DTap, was it alum? I don't really know, but I know that the combination was not good for her." Id. at 29 (citing Tr. at 88:5–9) (testimony of Dr. Sundel). She observed again that despite Dr. Sundel's critique of the ASIA theory, his "stated theory is based on the role of adjuvants in the development of adverse events." Id. Therefore, she stated, "[Dr. Sundel's theory] is ASIA and it fails now for the same reasons it has previously failed: the diagnostic criteria proposed by the ASIA study's authors are both vague and flawed." Id.

Drs. Sundel and Gurish's reports, she noted, "do not add precision to the ASIA criteria, elaborate on the role of aluminum or specify how much is needed, provide any further support from scientific or medical experts in the field, or add any additional evidence to support the theory." Id. at 30. In her view, Petitioner's experts merely "repeat[ed] what has already been rejected" in previous cases repudiating ASIA. Id. In short, the Special Master concluded, Petitioner "failed to provide a reputable medical theory" sufficient to prove Althen prong one because "she is unable to distinguish [her theory] from ASIA" and has "failed to present any new evidence to overcome" the "previously identified shortcomings" of ASIA. Id. at 31.

3. Althen Prong Two

The Special Master then turned to Althen prong two, which requires a petitioner to demonstrate a logical sequence of cause and effect showing the vaccination caused the injury. Id. at 32. According to the Special Master, Dr. Sundel's conclusion that A.F.'s sJIA was vaccine induced was grounded in the short period of time between vaccination and the onset of A.F.'s symptoms and on "the absence of alternative explanations" for her sJIA. Id. (quoting Pet'r's Ex.

[15] Dr. Gurish testified that he would "echo Dr. Sundel's opinion that while the ASIA hypothesis is intriguing in the sense that someone is trying to understand these adverse events on a very global scale," the ASIA hypothesis is "also is disruptive in the sense, for me as a scientist, it's hard to make predictions based on this global hypothesis . . . , and I want testable hypotheses to test, to try to prove whether there is a cause-and-effect relationship." Tr. at 127:24–128:7.

20 at 2). She noted, however, that "Petitioner's theory does not explain the roles any of the non-adjuvanted vaccines played in the development of A.F.'s sJIA," and that Petitioner's experts did not say which vaccines were necessary to cause A.F. to manifest symptoms. Id.

The Special Master asserted that Dr. Gurish had stated in his report that the symptoms A.F. experienced "two to four days after vaccination . . . match both the ASIA criteria and data from several studies." Id. (citing Pet'r's Ex. 29 at 5). She observed that "ASIA's diagnostic criteria are unclear" and concluded that "Petitioner has failed to provide preponderant evidence establishing that ASIA (or the ASIA-like theory proposed by Dr. Sundel) can be applied to any specific case generally, or A.F.'s specifically." Id. at 32–33.

The Special Master also found unavailing Dr. Sundel's testimony that A.F.'s sJIA was caused by a "confluence of events," including "her genetic predisposition and a variety of environmental factors." Id. at 33. She found more persuasive the alternative theory of causation proposed by the government's experts—that A.F.'s sJIA was triggered by a viral infection. Id. She cited their testimony that the effects of the small amount of aluminum contained in the vaccines are both localized and short lived and therefore "A.F.'s sJIA could not have been caused by her vaccines." Id. (citing Resp't's Ex. A at 7–8, ECF No. 32-1 (Expert Report of Dr. Rose); Resp't's Ex. J at 11–12). Further, she observed, they had opined that "A.F.'s genetic predisposition and MAS, which are both commonly triggered by viral infections, support the need for an 'ongoing driver' that gives rise to sJIA." Id. In addition, she noted that the government's experts had "also explained that because of A.F.'s genetic predisposition to sJIA—which is linked to the innate immune system via the cytolysis pathway—a similar MAS-like or JIA-like response would have occurred after every vaccination with an aluminum adjuvant." Id. As this did not occur, the Special Master found it "more likely that a viral infection triggered A.F.'s sJIA." Id.

The Special Master also found credible Dr. Rose's explanation that since A.F.'s lab results did not support the existence of MAS on March 27, 2009, the more likely explanation for A.F.'s purpuric rash was a viral infection. Id. And, the Special Master found, "[g]iven A.F.'s genetic predisposition and the symptoms she exhibited at the time, it is more likely that this viral infection was the substantial factor that triggered her sJIA than the vaccines in question." Id.

4. Althen Prong Three

Turning to prong three of the Althen test, which requires a petitioner to show a proximate temporal relationship between vaccination and injury, the Special Master observed that the parties disagreed on whether A.F.'s sJIA developed in mid-to-late March, i.e., within days after she was vaccinated on March 13, 2009, or whether its onset occurred weeks later, in early April 2009. Id. at 34. Dr. Sundel's "proposed time frame for disease onset was four to five days post vaccination," the Special Master wrote, which he based on A.F.'s medical records and her ultimate diagnosis of sJIA. Id. (citing Tr. at 19:13–17). According to the Special Master, this theory was based on "circular reasoning." Id. In her view, Dr. Sundel had posited "that because A.F.'s injury is vaccine induced, the onset of A.F.'s symptoms establishes the appropriate time frame for a vaccine-related injury." Id.

The Special Master observed, however, that the government's expert, Dr. Rose, did not believe that the purpuric rash A.F. had on March 27 was a symptom of sJIA, and that he had found that she did not have diagnosable MAS at that time. Id. Dr. Rose concluded on the basis of lab results that A.F.'s initial rash was caused by a viral infection, "which would place the onset for sJIA, weeks later, in early April 2009." Id. The Special Master found that "based on the preponderant standard, A.F.'s sJIA was more likely caused by a viral infection [and t]he time frame proposed by Dr. Rose is therefore more appropriate." Id.

The Special Master explained that neither party had offered medical literature that discussed an appropriate time frame for vaccine-induced sJIA. Id. It was therefore "[t]he broader deficiencies with Petitioner's theory (which did not otherwise establish that the DTaP and IP vaccines could cause sJIA) [that] render[ed her] unable to find that the timing at issue in this case of the alleged vaccine-induced sJIA has been shown to be medically acceptable." Id.

D. The Present Motion for Review

Petitioner filed her motion for review of the Special Master's Decision with this Court on July 17, 2019. Petitioner's Mot. for Review ("Pet'r's Mot."), ECF No. 121. In her motion, Petitioner argues that the Special Master "improperly heightened" her burden of proof, "and failed to consider the record as a whole." Id. at 13. Specifically, according to Petitioner, the Special Master required Petitioner to prove what she characterizes as a new "nebulous" theory, known as ASIA, that links adjuvanted vaccines to autoinflammatory diseases. Id. She also contends that the Special Master required "proof of the exact amount of the aluminum adjuvant needed to cause [s]JIA." Id. at 23. Finally, Petitioner argues that the Special Master committed legal error by requiring greater evidence from Petitioner than that articulated in Althen prong three, and that the Special Master failed to consider the record as a whole in denying entitlement based on the government's alternative theory of viral causation, which Petitioner contends is not supported by the evidence. Id. at 25–26.

The government filed its response to Petitioner's motion on August 16, 2019. Resp't's Mem. in Resp. to Pet'r's Mot. for Review, ECF No. 125. It argues that the Special Master properly identified and applied the legal standard, that Petitioner failed to establish a logical sequence of causation between the vaccines and the onset of A.F.'s injury, and that Petitioner did not establish that the timing between vaccination and the onset of her sJIA was medically appropriate. Id. at 9, 15, 17.

Oral argument was held on December 4, 2019. See ECF No. 127.

DISCUSSION

I. Jurisdiction and Standard of Review

Congress established the National Vaccine Injury Compensation Program in 1986 to provide a no-fault compensation system for vaccine-related injuries and deaths. Figueroa v. Sec'y of Health & Human Servs., 715 F.3d 1314, 1316–17 (Fed. Cir. 2013). The Vaccine Act is remedial legislation that should be construed in a manner effectuating its underlying spirit and purpose. Id.

A petition seeking compensation under the Vaccine Act is filed in the Court of Federal Claims, after which the Clerk of Court forwards it to the chief special master for assignment to a special master. 42 U.S.C. § 300aa-11(a)(1). The special master to whom the petition is assigned "issue[s] a decision on such petition with respect to whether compensation is to be provided under the [Vaccine Act] Program and the amount of such compensation." Id. § 300aa-12(d)(3)(A).

The Vaccine Act grants the Court of Federal Claims jurisdiction to review the record of the proceedings before a special master, and authority, upon such review, to:

1) Uphold the findings of fact and conclusions of law of the special master and sustain the special master's decision;

2) Set aside any findings of fact or conclusion of law of the special master found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law; or

3) Remand the petition to the special master for further action in accordance with the Court's direction. Id. § 300aa-12(e); see also Vaccine Rule 27.

On review of the special master's decision, the Court applies the arbitrary and capricious standard to factual findings and the "not in accordance with law" standard to legal rulings. Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010). The Court's scope of review is a narrow one. The Court "do[es] not reweigh the factual evidence, assess whether the special master correctly evaluated the evidence, or examine the probative value of the evidence or the credibility of the witnesses," because those "are all matters within the purview of the fact finder." Porter v. Sec'y of Health & Human Servs., 663 F.3d 1242, 1249 (Fed. Cir. 2011) (citing Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1345 (Fed. Cir. 2010)). "[A]s long as a special master's finding . . . is 'based on evidence in the record that [is] not wholly implausible,'" the Court must uphold it. Id. (quoting Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1338 (Fed. Cir. 2010) (alteration in original)). "'[T]he standard of review is uniquely deferential'" to a special master's decisions. Milik v. Sec'y of Health & Human Servs., 822 F.3d 1367, 1376 (Fed. Cir. 2016) (quoting Hodges v. Sec'y of Health & Human Servs., 9 F.3d 958, 961 (Fed. Cir. 1993). If a special master "'has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision,' then reversible error is 'extremely difficult to demonstrate.'" Milik, 822 F.3d at 1376 (quoting Hines v. Sec'y of Health & Human Servs., 940 F.2d 1518, 1528 (Fed. Cir. 1991)).

II. Petitioner's Burden of Proving Causation

To secure compensation under the Vaccine Act, a petitioner must prove by a preponderance of the evidence that the injury at issue was caused by a vaccine. See 42 U.S.C. §§ 300aa-11(c)(1), -13(a)(1). Where a petitioner sustains an injury in association with a vaccine listed in the Vaccine Injury Table, causation is presumed. Broekelschen, 618 F.3d at 1341–42 (citing 42 U.S.C. § 300aa-11(c)(1)(C)(i)); Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1374 (Fed. Cir. 2009)). Where, as in this case, the injury is not listed in the Table, the

petitioner must prove causation in fact. Broekelschen, 618 F.3d at 1342 (citing Moberly, 592 F.3d at 1321). To discharge that burden, "a petitioner must show that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Stone v. Sec'y of Health & Human Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) (quotations omitted). "Once the petitioner has demonstrated causation, she is entitled to compensation unless the government can show by a preponderance of the evidence that the injury is due to factors unrelated to the vaccine." Broekelschen, 618 F.3d at 1342 (citing Doe v. Sec'y of Health & Human Servs., 601 F.3d 1349, 1351 (Fed. Cir. 2010); see also 42 U.S.C. § 300aa-13(a)(1)(B)).

The three-pronged test that the Federal Circuit announced in Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274 (Fed. Cir. 2005), guides the causation determination. Under that test, to make a prima facie case that a vaccination caused the petitioner's injury, he or she must provide: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Id. at 1278. If Petitioner makes her prima facie case under Althen, the burden of proof shifts to the government "to establish that [a] factor unrelated to the vaccination is the more likely or principal cause of the injury alleged." Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs., 717 F.3d 1363, 1369 (Fed. Cir. 2013).

III. Merits of the Motion for Review

In this case, Petitioner argues that the Special Master "improperly heightened" her burden of proving causation. Pet'r's Mot. at 13. Specifically, she contends that the Special Master faulted her for failing to address and resolve the apparent flaws of the ASIA theory, notwithstanding that her experts articulated a narrower theory of causation specific to A.F. Id. She further contends that the Special Master failed to consider the record as a whole and instead premised her denial of entitlement "on the Petitioner's failure to prove a different and much larger theory"—i.e. ASIA. Id. at 22.

For the reasons set forth below, the Court agrees with Petitioner that the Special Master's decision includes passages in which she appears to have conflated Petitioner's specific theory of causation with the more generic "ASIA theory," which prior decisions under the Vaccine Act have found too vague and overbroad to support a causal relationship between vaccines and autoimmune or autoinflammatory diseases. See Dec. at 29–30 (listing cases). Nonetheless, the Court concludes that the error was a harmless one because, as explained below, the Special Master's decision reflects that she also found that Petitioner failed to show by preponderant evidence that the specific theory of causation her experts articulated satisfied prongs one and/or two of the Althen test. Because those findings are "based on evidence in the record that [is] not wholly implausible," they must be affirmed. See Porter, 663 F.3d at 1249.[16]

[16] Because the Court sustains the Special Master's findings regarding Althen prongs one and two, it does not address Petitioner's claims regarding the Special Master's analysis under prong three.

A. The Special Master's Decision Reflects Some Conflation of Petitioner's Specific Theory of Causation with the More Generic ASIA Theory

As the Special Master observed, to satisfy prong one of the Althen test, Petitioner was required to set forth a medical theory explaining how the vaccines A.F. received could have caused her injury. Dec. at 26–27. (citing Pafford v. Sec'y of Health & Human Servs., No. 01-01765V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004) aff'd sub nom. Pafford ex rel. Pafford v. Sec'y of Health & Human Servs., 64 Fed. Cl. 19 (2005), and aff'd sub nom. Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352 (Fed. Cir. 2006)) (noting that prong one addresses whether the vaccine at issue can cause the type of injury alleged). To pass muster, the theory had to be more than merely "plausible" or "possible." Boatmon v. Sec'y Health & Human Servs., 941 F.3d 1351, 1360 (Fed. Cir. 2019). Instead it was required to be both "sound and reliable," Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548 (Fed. Cir. 1994), and to rise to the level of more probable than not, Moberly, 592 F.3d at 1322; see also Althen, 418 F.3d at 1279.

Petitioner's medical theory regarding causation is based on sJIA's characterization as an autoinflammatory disease triggered by activation of the innate, rather than the adaptive, arm of the immune system. This characterization of sJIA is not in dispute. See, e.g., Tr. at 172:1–4 (testimony of Dr. Rose that sJIA is an autoinflammatory, not autoimmune, disease); Resp't's Ex. A at 11 (expert report of Dr. Rose stating that autoinflammatory diseases are "associated with pathogenic pathways of the innate immunity"); Tr. at 238:1–3, 15–18 (testimony of Dr. Whitton that the "pathogenesis of [sJIA] is driven by the innate immune system" and is "autoinflammatory"). Also not in dispute is the fact that "cytokines . . . aris[ing] out of the innate immune system . . . [lead] to the symptoms of sJIA." Id. at 182:2–5, 13–16 (testimony of Dr. Rose).

All of the testifying experts also agreed on another essential element of Petitioner's theory of causation: that aluminum "stimulate[s] the innate immune system." Id. at 114:24–25 (testimony of Dr. Gurish); see id. at 200:23–25 (testimony of Dr. Whitton concurring that there is "no question [that] alum, as well as other adjuvants, activate the innate immune system"). Dr. Rose acknowledged that "cytokines are generated after immunizations." Id. at 184:13–18. Dr. Whitton similarly testified that he "fundamentally . . . agree[d]" that "alum is internalized by macrophages, [] activates the macrophages, [and] . . . rapidly triggers [] cytokine production by the macrophages." Id. at 201:14–17.

Finally, experts for both parties also agreed: 1) that the precise cause of sJIA is unknown, Resp't's Ex. A at 9–10 (report of Dr. Rose stating that sJIA's "relationship with presumptive triggers" as well as which triggers are necessary for disease onset are unknown), and 2) that its occurrence in any particular individual requires a "confluence of events," namely a combination of genetic susceptibility and environmental triggers, Tr. at 172:7–9, 173:16–20, 174:6–13 (testimony of Dr. Rose); see also Resp't's Ex. G at 6 (expert report of Dr. Rose).

Petitioner's experts proposed a theory of causation that was based on these agreed-upon principles and that took into consideration A.F.'s particular characteristics and medical history. Dr. Sundel's opinion was that in A.F.'s case, the sJIA was triggered by a "combination of factors" which included her "genetic[] susceptib[ility]," a change in her "microbiome . . .

because her diet was different," her recent ear infection, which "activate[d] the adaptive immune system," and her recent treatment with "amoxicillin . . . [which has] effects on the innate immune system." Tr. at 42:16–17, 43:10–44:1. As the Special Master observed, according to Dr. Sundel, A.F.'s condition was akin to "'a bubbling pot' created by a combination of her genetic predisposition and a variety of environmental factors, with the vaccines being a 'brick [thrown] into [the pot] and it overflowed.'" Dec. at 21 (quoting Tr. at 53:9–25). Put another way, Dr. Sundel testified that the immunization acted as "the ultimate hammer blast . . . which provided the alum which stimulated her innate immune system . . . [and] the DTaP and the polio vaccine, which were all antigens which stimulated both the innate and adaptive immune system." Tr. at 44:2–9. Having all of the components of the vaccine administered to A.F. "at the same time," he opined, was "sufficient to increase [A.F.'s] levels of inflammation" beyond that which her body could control. Id. at 304:9–16.

In short, Petitioner's experts articulated a specific theory of causation that involves a specific adjuvant (aluminum), the etiology of a specific auto-inflammatory disease (sJIA), and A.F.'s own pertinent medical history. The ASIA theory, on the other hand, sets forth a much more global hypothesis: that a "genetically susceptible subject may develop either an autoimmune or auto-inflammatory disease . . . following exposure" to an "adjuvant[] (i.e. silicone, alum, pristane, infectious components)." Pet'r's Ex. 23, Tab D at 37 (Shoenfeld article). It proposes that there may be links between exposure to these various adjuvants and the occurrence of a number of different autoimmune/autoinflammatory diseases and conditions, including siliconosis, Gulf War syndrome, macrophagic myofascitis syndrome, and a variety of "post-vaccination phenomena." Id.

The ASIA theory does not propose any specific timetable for the onset of symptoms after exposure to an adjuvant. It hypothesizes that "vaccines can induce . . . inflammatory condition[s] and overt autoimmune disease[s] . . . weeks and even months or years following vaccination." Id. at 38. Further, the Shoenfeld article provided that ASIA "syndrome" could be identified on the basis of a variety of vague and unspecific diagnostic criteria. Id. at 37, 40. These included: 1) "exposure to a variety of external stimuli (infection, vaccine, silicone, adjuvant)"; and 2) "the appearance of 'typical' clinical manifestations," including: "[a]rthralgia and/or arthritis," "[c]hronic fatigue, un-refreshing sleep or sleep disturbances," "[n]eurological manifestations," "[c]ognitive impairment, memory loss," and "[p]yrexia, dry mouth." Id. at 40.

Petitioner's theory is distinct from ASIA in a number of respects. First, it is based on uncontroverted processes linked to auto-inflammatory diseases, like sJIA, and makes no claims about autoimmune diseases. Second, Petitioner's expert testimony and literature extensively discusses the role of the aluminum adjuvant on the body, and not just the role of adjuvants more generally. Third, Petitioner's experts allege that their theory encapsulates the larger immunologic effect of the antigen within the vaccine. See, e.g., Tr. at 33:21–34:9, 304:8–16 (testimony of Dr. Sundel). Fourth, Petitioner's theory of causation provides a specific timetable for the onset of symptoms following vaccination positing the onset of sJIA within two to six days after exposure to an alum adjuvant in combination with the antigens in the vaccine.

Finally, Petitioner's theory is based on the impact of the vaccine as a "hammer blow" struck in the context of her genetic susceptibility and a host of other environmental factors that had upregulated primarily her innate, but also her adaptive, immune system. The impact of some

of these environmental factors, such as her ear infection and her antibiotic treatment, are undisputed by the government's experts. She does not seek to prove her theory on the basis of ASIA's diagnostic criteria.

Because of the particularized nature of Petitioner's theory of causation in this case, the ASIA-related cases the Special Master cited, see Dec. at 29, are inapposite. In D'Angiolini v. Secretary of Health and Human Services, for example, the court affirmed the Special Master's rejection of a petitioner's argument that his child suffered from "ASIA syndrome" because research on ASIA was still preliminary and incomplete and because its criteria were currently so "'ill-defined . . . that it makes it very difficult to . . . make [a] diagnosis.'" 122 Fed. Cl. 86, 95 (2015), aff'd, 645 F. App'x 1002 (Fed. Cir. 2016) (quoting testimony of the government's expert).

The special master in Garner v. Secretary of Health and Human Services rejected petitioner's reliance on ASIA to support a showing of causation where the date of the onset of petitioner's autoimmune disease was forty-five days after vaccination. No. 15-063V, 2017 WL 1713184, at *16 (Fed. Cl. Spec. Mstr. Mar. 24, 2017), aff'd, 133 Fed. Cl. 140 (2017). He observed that ASIA "defines virtually any length of time passing between vaccine receipt and injury as medically appropriate—a concept antithetical to the legal rationale for the third Althen prong." Id. at *17. In Rowan v. Secretary of Health and Human Services, the special master similarly rejected the ASIA-based theory that the alum adjuvant could cause chronic headaches that began several months after vaccination. No. 10-272V, 2014 WL 7465661, at *8 (Fed. Cl. Spec. Mstr. Dec. 8, 2014). And in another case where the injury onset did not occur until several months following vaccination, the special master rejected a theory of causation that was based on the what he characterized as the assertions of the originator of the ASIA theory (Dr. Shoenfeld) that "all adjuvants are basically the same," that "all autoimmune diseases are the same," and that "the only timing that is relevant is that the disease came after the vaccine and not before." Johnson v. Sec'y of Health & Human Servs., No. 10-578V, 2016 WL 4917548, at *8 (Fed. Cl. Spec. Mstr. Aug. 18, 2016) (internal quotation marks omitted).

In this case, Petitioner's experts did not contend that A.F. suffered from ASIA syndrome, as did the petitioner in D'Angiolini. Nor did they purport to use ASIA theory to reconcile the amount of time that elapsed between A.F.'s vaccination and the onset of her sJIA, as did the petitioners in the other cases the Special Master cited. To the contrary, their theory posits a reasonable time period between vaccination and onset of two to six days. In addition, they were careful to separate and distinguish their theories from ASIA and, as noted, even rejected ASIA as "too broad for a theory that will have any use in clinical medicine." Tr. at 84:20–22. Indeed, like the Special Master herself, they concluded that its diagnostic criteria are not useful because they are vague and overbroad. See id. at 127:24–129:2.

Further, the fact that Petitioner's experts referenced ASIA or studies designed to test its hypothesis in their reports or testimony does not mean—as the Special Master found—that their theory "is" ASIA. See Dec. at 29. That misperception caused the Special Master to impose some evidentiary requirements on Petitioner that were inappropriate. For example, in assessing the relative credibility of the parties' experts, the Special Master was critical of Dr. Sundel for not "refer[ring] to his theory by the ASIA acronym well known in the program . . . [d]espite his clear assertion that sJIA is an autoimmune syndrome induced by adjuvants." Id. at 28. She also was

critical of Dr. Gurish for "not explain[ing] away holes in the [ASIA] causation theory that relate to its vague symptoms or unspecific triggers." Id. at 29.

Similarly, in conducting her prong one analysis, the Special Master held that Petitioner's theory of causation "fails now for the same reasons it has previously failed: the diagnostic criteria proposed by the ASIA study's authors are both vague and flawed." Id. In support of her conclusion as to prong one, she cited the cases set forth above, which, as the Court has explained, are inapposite. She challenged the Petitioner's theory on the grounds that, among other things, her experts "d[id] not add precision to the ASIA criteria," or "elaborate on the role of aluminum or specify how much is needed." Id. at 30. In addition, the Special Master criticized Petitioner's experts for not providing evidence to overcome their own critiques of the ASIA theory. Id. at 31.

The Special Master's supposition that Petitioner's theory was synonymous with ASIA also affected her Althen prong two analysis. In particular, she criticized Dr. Gurish on the grounds that he had argued that the symptoms A.F. developed four days after vaccination "match both the ASIA criteria and data from several studies." Id. at 32 (citing Pet'r's Ex. 29 at 5). The Special Master then engaged in a critique of the overbreadth and generality of ASIA's diagnostic criteria. Id. at 32–33. But in evaluating Dr. Gurish's Expert Report cited by the Special Master, the Court did not find any passage in which Dr. Gurish purported to match A.F.'s symptoms to the ASIA criteria. See Pet'r's Ex. 29 at 5. Instead, his report consists of an overview of the mechanics of the immune system, the effects of vaccinations on the immune system, the etiology and nature of sJIA, and his opinion regarding the particular events that he concluded led A.F. to develop sJIA, with citation to what he argued were supporting studies.

B. The Special Master's Error Was a Harmless One

Notwithstanding the foregoing, the Court concludes that the Special Master's erroneous conflation of Petitioner's theory of causation with the ASIA hypothesis constituted harmless error. It was not outcome determinative because the Special Master's findings also reflect that she found Petitioner's specific theory of causation unpersuasive independent of her findings regarding Petitioner's failure to prove ASIA's validity. In other words, the conclusion the Special Master reached—that Petitioner failed to satisfy prongs one and/or two of Althen—would have been the same even if she had not, in some respects, conflated the theory articulated by Petitioner's experts with ASIA as described above. Because her findings were based on the record as a whole and were not unreasonable, her decision must be sustained. See Broekelschen, 618 F.3d at 1350 (citing Hines ex rel. Sevier v. Sec'y of Health & Human Servs., 940 F.2d 1518, 1526 (Fed. Cir. 1991)) (finding that the special master's improper consideration of certain evidence regarding causation was harmless error where his decision was based on a number of factors and petitioner did not show that consideration of the evidence was "likely critical to the result"); Tebcherani ex rel. Tebcherani v. Sec'y of Health & Human Servs., 55 Fed. Cl. 460, 476 (2003) (holding that the court was "constrained to find . . . errors to be harmless in this case, because neither the Special Master's inappropriate reference to the presence of an alleged viral illness nor the improper assignment of the burden of proof impacted the ultimate decision in this matter"); Johnson v. Sec'y of Health & Human Servs., 33 Fed. Cl. 712, 728 (1995), aff'd, 99 F.3d 1160 (Fed. Cir. 1996) (finding the failure to consider an expert report was harmless where the report did not contain evidence "that [was] sufficiently detailed or probative of the causation

issue to change the outcome determined by the special master"); Cox v. Sec'y of Health & Human Servs., 30 Fed. Cl. 136, 143 (1993) (stating that "while the special master abused his discretion by striking" an expert's medical report from the record, "it was harmless error to do so," because the court's own review of that report showed that it "deserve[d] little or no weight in light of the entire record").

1. The Special Master Reasonably Found that Petitioner Did Not Prove the Validity of Her Specific Theory of Causation

First, the Special Master reasonably found that Petitioner had failed to meet her burden under Althen prong one to establish a medical theory causally connecting the vaccination and the injury. She discredited the specific theory proposed by Petitioner's experts because she concluded: 1) that it "does not explain the roles any of the non-adjuvanted vaccines played in the development of A.F.'s sJIA," and 2) that it does not identify "which . . . vaccines were needed for A.F.'s symptoms to manifest." Dec. at 32. "In fact," the Special Master observed, "Dr. Sundel "[did] not apply his theory to the specific vaccinations that A.F. received." Id.

The Special Master found Dr. Sundel's expert testimony undermined by his equivocation and lack of clarity on these points. Id. at 28 (citing Tr. at 88:5–9) (observing that petitioner's medical theory "can best be summed up by Dr. Sundel's assertion, 'was it the IP[vaccine], was it the DTap, was it the alum? I don't really know but I know that the combination was not good for her.'"). The Special Master is, of course, "entitled—indeed, expected" to make such determinations concerning "the reliability of the evidence presented to [her] and, if appropriate, as to the credibility of the persons presenting the evidence." See Moberly, 592 F.3d at 1326. And the Court's role in reviewing such determinations is an exceedingly narrow one.

The Court finds unpersuasive Petitioner's argument that the Special Master improperly required her to prove the "exact quantity" of aluminum necessary to trigger sJIA. See Pet'r's Mot. at 23. According to Petitioner, this imposed a requirement that she supply direct evidence of causation when circumstantial evidence should be sufficient. Id. But the Special Master did not base her rejection of Petitioner's theory of causation on the failure of Petitioner's experts to prove the precise amount of aluminum needed to trigger sJIA. She merely identified the fact that Petitioner's experts did not "elaborate on the role of aluminum or specify how much is needed," as one of a number of flaws and/or unanswered questions raised by their theory of causation. Dec. at 30.

The Special Master further cast doubt on the probative value of many of the studies upon which Petitioner's experts relied, including the study Dr. Sundel referenced when asked for his "best evidence that aluminum salt can trigger pathological inflammation or another adverse event." Dec. at 28 (citing Tr. at 82:1–18). Dr. Sundel had opined that the Cerpa-Cruz et al. study, supra, supports the role of aluminum adjuvants "particularly in young girls who develop arthritis shortly after an immunization," Dec. at 10 (citing Pet'r's Ex. 23, Tab L). Citing Dr. Whitton, one of the government's experts, the Special Master found that this study "suffers from serious limitations." Id. at 30. Specifically, it "included no control group, its population size was small, and there was an inherent selection bias." Id. She noted that Dr. Gurish (and the study's own authors) had conceded that "the study's retrospective design and lack of control group make it impossible 'to prove causal correlation between sJIA alone and the various vaccines analyzed.'"

Id. (citing Pet'r's Ex. 23, Tab L at 5). The Special Master concluded that, given these deficiencies, "the study does not provide persuasive support, under the preponderant standard, for the contention that aluminum-adjuvated vaccines can cause sJIA." Id.

Finally, the Special Master credited the testimony of the government's experts that A.F.'s sJIA could not have been caused by her vaccines "because the effects of the small amount of aluminum contained in the vaccines in question are localized and short lived." Id. at 33. This finding was critical because while the parties' experts agreed on the existence of the underlying biological mechanism which causes adjuvants to stimulate the innate immune system, they disagreed on whether or not the stimulation caused by adjuvants was too transient and short lived to trigger the onset of sJIA.

Dr. Whitton opined that aluminum's triggering effect on the innate immune system, including cytokine production, occurs "usually within the first 24 to 48 hours and [then] dissipate[s] fairly rapidly thereafter." Tr. at 202:15–20. In support, he cited a study that he stated demonstrated that the effect of the adjuvant, and thus its ability to trigger an immune response, is "local" and "short-lived." Id. at 206:13–14; see id. at 204:4–206:18.[17] In his view, an adjuvant's transient effect was insufficient to "drive a serious autoinflammatory disease." Resp't's Ex. J at 8–9.

Petitioner's expert, Dr. Gurish, acknowledged that aluminum must provide an ongoing driver of inflammation to trigger sJIA. Pet'r's Ex. 29 at 7. In his view, however, alum may supply such a driver because it is "taken up by macrophages," which he stated "translocate" and are "found containing alum throughout the body." Tr. at 106:18–107:2. But when asked for his "best evidence that the alum distributed around the body is pathogenic," id. at 125:7–18, Dr. Gurish cited a study that "involved the administration of high doses of aluminum in sheep over a prolonged period of time," i.e., Lluis Lujan et al., Autoimmune/Autoinflammatory Syndrome Induced by Adjuvants (ASIA) Syndrome in Commercial Sheep, 56 Immunol. Research 317 (2013), Dec. at 31 (citing Resp't's Ex. K at 5, 8, ECF No. 86-1) (Second Supplemental Expert Report of Dr. Whitton). Dr. Whitton criticized the study's probative value, observing that "the sheep were given a combination of fourteen different vaccines," which he opined made it "impossible to determine whether a specific vaccine, if any, was responsible for adjuvant-related complications." Dec. at 31. The Special Master concluded that "Dr. Whitton's critiques effectively render the study and its findings inapposite because it cannot link sJIA with a specific vaccine and/or adjuvant." Id. She also criticized Dr. Gurish for comparing "a single adjuvanted

[17] In the study, Dr. Whitton reported, antigen was injected into one leg of a mouse and "a slightly different adjuvant" than alum was injected into the opposite leg, and this resulted in no immune response. Tr. at 204:15–205:6. To Dr. Whitton, if petitioner's notion that "systemically distributed alum has a biological impact" was correct, then there would have been "an immune response to the antigen." Id. at 205:6–14. The study also showed that the effect of the adjuvant was "short-lived," according to Dr. Whitton, because no immune response occurred when an antigen was injected in the same anatomical spot twenty-four hours after the adjuvant injection, indicating that "the immunostimulatory effect of the adjuvant has gone." Id. at 206:2–4, 12–18.

vaccine to aluminum hydroxide content so high that the study's authors were concerned about possible cytotoxicity." Id.

Similarly, the Special Master rejected Dr. Gurish's reliance upon the Bagavant article to support his theory that alum can "enhance[] autoimmune response in individuals with a specific genetic disposition to . . . an autoimmune disease." Id. at 31 (citing Harini Bagavant et al., Alum, an Aluminum-based Adjuvant, Induces Sjögren's Syndrome-like Disorder in Mice, 32 Clin. & Exper. Rheum. 251 (2014)). She noted several limitations to the study, including that "the mice were dosed [with alum] using routes of administration other than the intramuscular route used when administering vaccines to humans" and that the high dose of alum administered meant that the "study's findings could also be explained by aluminum toxicity rather than the vaccination." Dec. at 31.[18]

Finally, the Court notes that even if it might have reached a different conclusion had it considered the evidence on a de novo basis, its scope of review of the Special Master's Decision is a very narrow one.. See Paterek v. Sec'y of Health & Human Servs., 527 F. App'x 875, 882 (Fed. Cir. 2013) (holding that it was legal error for the court of federal claims to "reevaluate[] the evidence and c[ome] to its own findings," especially regarding fact-intensive conclusions where the "medical evidence of causation is in dispute"). The Special Master's finding that Petitioner had failed to establish by preponderant evidence a medical theory causally connecting the vaccination and the injury was based on the record as a whole, adequately explained, and not unreasonable. The Court therefore sustains the Special Master's decision that Petitioner did not meet her burden of proof under Althen prong one.

2. Althen Prong Two

In addition to finding that Petitioner failed to show a medical theory that causally connected A.F.'s development of sJIA to the vaccines she received, the Special Master also found that the Petitioner failed to show by preponderant evidence "a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Dec. at 34 (quoting

[18] At oral argument, Petitioner's counsel asserted that the Special Master failed to discuss Petitioner's counter evidence on the amount of aluminum the mice in the Bagavant study received when compared to the amount a human would receive. Oral Arg. at 2:14:05–2:14:45. The Special Master in discrediting the Bagavant study cited Dr. Whitton's statement from his expert report that "'when corrected for body weight, the[study] mice appear to have been given around . . . [nine hundred and twenty-four thousand] times the dose that is given in a human vaccine.'" Dec. at 31 (quoting Resp't's Ex. K at 8). The Court agrees with Plaintiff that the Special Master failed to note that in testimony, Dr. Whitton stated he "ha[d] to now correct" this number in A.F.'s case and stated instead that the researchers "gave [the mice] roughly 300,000 times more alum on a weight-for-weight basis than were given to humans," Tr. at 215:7–21, and that she further failed to address Dr. Gurish's counter contention that the dose is only "to the order of 10 to 50 times" higher than the dose used in humans, Tr. at 322:19–20. It is unnecessary for the Court to resolve this disagreement because the Special Master also rejected the article's probative value based on the differences between the routes of alum administration to the mice in the study versus the intramuscular route used to administer vaccines.

Althen, 418 F.3d at 1278). The Court concludes that the Special Master's denial of entitlement is independently sustainable on that ground because she considered the evidence of record relevant to that finding, drew plausible inferences, and articulated a rational basis for her determination.

The Special Master concluded that the Petitioner did not prove that the vaccination was the reason for A.F.'s injury because she found that the government's experts had "argued persuasively that the facts of this case are more consistent with an alternative cause" for the triggering of A.F.'s sJIA—namely, "a viral infection." Id. at 33. Dr. Whitton, for example, found it more biologically plausible that a virus caused A.F.'s sJIA because of his view, discussed above, that "autoinflammatory disease requires an ongoing driver of inflammation." Resp't's Ex. J at 8. Alum, he testified, "cannot replicate," so whatever amount of alum is injected into a person is the "maximum." Tr. at 207:2–4. A virus, by contrast, is "massively replicating" and "a single viral particle" could replicate into "billions of copies" within "24 hours." Id. at 208:3–13. Dr. Whitton opined that an individual could therefore have a "very profound innate immune response to virus infection." Id. at 209:21–22. He concluded that a viral infection would therefore be "more likely" than the alum adjuvant "to cause havoc in someone with a genetic susceptibility to [MAS]." Id. at 226:19–25.

Dr. Rose similarly opined that it was more "plausible" that a "viral infection" initiated the onset of A.F.'s sJIA. Resp't's Ex. A at 15. At the outset, he noted that A.F. had experienced an ear infection before she was vaccinated. Id. at 7. After analyzing her March 24, 2009 lab results, Dr. Rose testified that "any clinician" would say that A.F.'s cell count "suggests a viral infection" and is "[d]efinitely not the cell count of [s]JIA," Tr. at 146:16–20; 147:10–13. Moreover, he testified that MAS, with which A.F. was diagnosed in May 2009, "is overwhelmingly a post-viral phenomenon" and is "highly suggestive of carrying [the] genes that [cause] . . . an abnormal response to viral infections." Id. at 188:18–24. Hence, Dr. Rose opined in response to questioning by Petitioner's counsel that "A.F.'s fever, joint pain, [and] rash" at the end of March were caused by a virus. Id. at 191:2–7.[19]

Dr. Rose also testified that the "clinical features of the rash" A.F. developed on March 17, four days after her vaccination on March 13, were more consistent with a virus than with the rash that typically accompanies sJIA. Tr. at 145:20–21. He observed that until Dr. Kimura identified an sJIA rash on April 16, "at least three doctors . . . described a rash that does[not] fit the rash of [s]JIA [because of] the presence of petechiae and . . . purpura." Id. at 145:21–25. According to Dr. Rose, many viruses are capable of causing "petechiae or purpura." Id. at 178:13–19, 179:8–12. On the other hand, the purpuric nature of the rash would be "unusual" in cases of sJIA "except when the presentation of the disease coincides with an episode of [MAS]." Resp't's Ex. A at 6. But Dr. Rose opined that "based on laboratory results," A.F. "did not have diagnosable MAS on March 27," when the petechiae and purpura were observed by clinicians. Id.

[19] In his direct testimony, Dr. Rose testified that although in his view A.F.'s cell count and the nature of her rash in late March of 2009 were "two pieces of solid evidence that are beyond question that [A.F.] was experiencing a viral insult," she also "had joint pains" and "constitutional symptoms" that could have been attributable to sJIA.

Finally, Dr. Rose found it significant that prior vaccinations had not had a similar effect on A.F. As the Special Master noted, Dr. Rose had "explained that because of A.F.'s genetic predisposition to sJIA—which is linked to the innate immune system via the cytolysis pathway—a similar MAS-like or sJIA-like response would have occurred after every vaccination with an aluminum adjuvant." Dec. at 33 (citing Resp't's Ex. A at 16–17). The Special Master concluded that because there had not been similar responses to prior vaccinations, it was more likely that the immediate trigger for A.F.'s illness was a viral one.

In her motion for review, Petitioner contends that the Special Master ignored evidence and failed to consider the record as a whole when she adopted the position of the government's experts that a viral infection most likely triggered A.F.'s sJIA. Pet'r's Mot. at 26. Among other things, Petitioner asserts that the Special Master ignored that all of the tests administered to A.F. to check for viruses had come back negative and that none of the physicians who treated A.F. in the weeks after she was vaccinated diagnosed a viral infection. See id. at 27.

The Court does not agree that in finding a virus the more likely cause for the occurrence of sJIA in A.F., the Special Master ignored the fact that test results for viruses had come back negative. To the contrary, she acknowledged as much in her discussion of Dr. Rose's opinion. See Dec. at 24–25. The Special Master concluded that the negative test results were not dispositive, and that finding is supported by the testimony of the government's experts. Dr. Rose explained, for example, that in practice doctors only "test for the most common and the most likely [viruses] that [they] have a test for." Tr. at 171:17–18. Dr. Whitton similarly testified that there are not "available tests for all viruses," Id. at 223:8–10. He also testified that "often, by the time the disease is florid, the virus is gone." Id. at 223:10–11. Therefore, he said, "depending on what types of tests were done, and that's a very important qualifier, the tests may turn out negative." Id. at 223:14–16.

Petitioner also argues that the Special Master ignored Dr. Sundel's testimony that on March 20, when A.F. was first evaluated for her rash, she received prednisone, which Dr. Sundel testified is an "immunosuppressive drug" and therefore is not typically prescribed if the cause of the rash was "thought to be a bacterial . . . or viral infection." Id. at 275:23–25, 278:15–17. It is not prescribed because "in the case of a bacterial infection, steroids can actually worsen the outcome and increase the risk of morbidity and mortality." Id. at 278:22–25. Dr. Sundel concluded that based on his review of the record, A.F.'s treating physician on March 20 were "not thinking viral infection." Id. at 279:3–6.

Notwithstanding the prednisone prescription, there is other evidence in the record that seems to refute Dr. Sundel's statement that none of the physicians were "thinking viral infection" in the weeks following the vaccinations. See id. Indeed, as discussed above, A.F.'s doctors ordered tests that were intended to rule out a viral infection. Id. at 162:18–163:3. In addition, several of A.F.'s medical records demonstrate that her doctors did consider a viral diagnosis. See Pet'r's Ex. 3 at 3 (medical records from allergy and asthma center documenting an "Assessment" of either "allergic" or "viral"); Pet'r's Ex. 4 at 2 (medical records from Richmond Pediatrics noting an "Impression" of "viral[,] JRA, [or] HSP"). In any event, even if her treating physicians had not thought of the possibility that A.F. had a viral infection, the Special Master was entitled to credit Dr. Rose's opinions regarding the greater likelihood that a virus triggered A.F.'s sJIA

than the vaccine, particularly given her conclusion—also based on the opinion of the government's experts—that Petitioner's own theory of causation was flawed.

In short, the Special Master's finding that Petitioner had failed to prove by preponderant evidence that the vaccination caused A.F. to develop sJIA, and her conclusion that it was more likely caused by a viral infection, is supported by evidence in the record. The Special Master drew plausible inferences from the record and articulated a reasonable basis for her conclusion that Petitioner had failed to satisfy Althen prong two. For those reasons her decision must be sustained.

CONCLUSION

On the basis of the foregoing, Petitioner's motion for review is **DENIED** and the Decision of the Special Master is **SUSTAINED**. The Clerk is directed to enter judgment accordingly.

IT IS SO ORDERED.

s/ Elaine D. Kaplan
ELAINE D. KAPLAN
Judge